

REMARKS

Claims 1 and 3-27 are pending. No new matter has been added by way of the present amendment. For instance, claim 1 has been amended to replace the recitation of "to a targeting protein" with "with a targeting protein" as suggested by the Examiner. Additionally, the phrase "into one of the phases" has been clarified to recite "into one phase of said ATPS." The term "ATPS separation" of claim 1 has been replaced with "ATPS-mediated protein separation" as suggested by the Examiner. The dependency of claim 9 has been altered. Claim 11 has been amended to replace the recitation of "cellbound" with "cell bound." Additionally, claims 11 and 12 have been amended to reflect the particular nature of the "part" of said "cell bound protein" or said "extracellular protein" according to claims 11 and 12, respectively. A similar amendment has been made to claim 14 concerning the "part" of said antibody protein. Claim 19 has been amended to replace the recitations of "such proteins" and "such protein" with "the fusion protein." The dependency of claims 20 and 23 has been altered to depend upon claim 1. Also, other multiple dependency issues have been addressed in various claims. Claim 21 has been amended to provide sufficient antecedent basis for the "detergent-based aqueous two-phase system." Additionally, claim 22 has been amended

such that "thermoseparating" is one word and to define the nature of the polymer as a "polyethylene polypropylene copolymer." New claim 25 is supported by the present specification at page 6, lines 27-29 and new claim 26 is supported by the present specification at page 7, lines 23-28. Lastly, new claim 27 is supported by originally filed claim 1. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Objections to the Specification and the Claims

The Examiner has objected to the specification, for instance at page 13, line 13 and page 10, line 29. Applicants have provided the full name for the abbreviation SDS-PAGE as "sodium dodecyl sulphate polyacrylamide gel electrophoresis" and the full name for "HFBI" as "hydrophobin I." Accordingly, this objection is moot.

The Examiner has also objected to claim 1, item a), stating that "to a targeting protein" should be changed to "with a targeting protein." Applicants have adopted this suggestion.

The Examiner has also suggested that in claim 1, item b), "ATPS-separation" be changed to "ATPS-mediated separation."

Applicants submit that this phrase has been replaced with "ATPS-mediated protein separation."

The Examiner has suggested that "cellbound" in claim 10 be replaced with "cell bound." Applicants have adopted this suggestion.

The Examiner has objected to claims 21 and 23 for being improperly dependent. Applicants believe that the Examiner is referring to claims 20 and 23 and submit that the dependency of these claims has been addressed in the present amendment.

Lastly, the Examiner asserts that in claim 22 the recitation of "thermo separating polymer system" be replaced with "thermoseparating polymer system." This suggestion has been adopted.

Applicants have adopted each of the Examiner's suggested changes. Accordingly, each of the above objections are moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1, 3-5, 10-15 and 18-23 under 35 U.S.C. § 112, first paragraph, for the reasons recited at pages 4-6 of the outstanding Office Action. Applicants respectfully traverse this rejection. In particular, the Examiner asserts that

the rejected claims contain subject matter which is allegedly not supported by the specification and in particular, the Examiner asserts that these claims contain subject matter which was not described in the specification in such as way as to reasonable convey to one skilled in the art at the time the application was filed that Applicants had possession of the claimed invention. Applicants respectfully disagree with the Examiner.

The Examiner asserts that the "parts" of hydrophobin-like protein polypeptides has not been described in the specification and thus is not supported. Those of ordinary skill in the art understand that the "parts" refer to portions of hydrophobins or hydrophobin-like proteins. The specification describes examples of these molecules, for instance at page 7, line 23 to page 9, line 10. Based upon such discussion and the general knowledge in the art, Applicants respectfully submit that those of ordinary skill in the art fully understand that Applicants were in possession of the "parts" of the claimed hydrophobins and hydrophobin-like proteins. Further, the specification allows those of skill in the art to make and use the claimed subject matter.

Accordingly, Applicants respectfully submit that the Examiner's rejection is improper and should be withdrawn. Reconsideration and withdrawal of this rejection is respectfully requested.

The Examiner has also stated that the specification fails to describe "derivatives" of the aqueous two-phase system as recited in claim 20. Applicants traverse and submit that the term "derivatives" has been removed from this claim. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1, 3-5, 10-15 and 18-23 under 35 U.S.C. § 112, second paragraph, for the reasons recited at pages 6-7 of the outstanding Office Action. Applicants respectfully traverse each of these rejections.

First, the Examiner has rejected claim 1 for the recitation of "combining a protein... to a targeting protein...." The Examiner asserts that the recitation is unclear as to whether or not the "combining" refers to recombinant fusion or non-covalent combination between the protein and the targeting protein. Further, the Examiner asserts that the term "and parts thereof" is indefinite. Applicants traverse. As explained in the present specification at page 6, lines 19-23, the "combining" can be performed by any method, for instance by genetic tagging of proteins, by chemical binding, gluing or by use of any other technique. Accordingly, the language

referred to by the Examiner is fully understood by one of ordinary skill in the art. Further, as discussed above, the "parts" referred to in the claims are fully understood by those of skill and are thus definite.

Second, the Examiner has rejected the recitation of "an ATPS separation" in claim 1, suggesting it be replaced with "an ATPS-mediated protein separation." Applicants have adopted this suggestion.

Third, the Examiner has rejected claim 14 for recitation "a part thereof" and has inquired as to whether or not the "part" refers to a fragment of the recited antibody or a ligand that binds to the antibody protein. Applicants traverse and submit that claim 14 has been amended to clarify that the "part" refers to the part of the antibody protein. Similar amendments have been made to claims 11 and 12.

Fourth, the Examiner has rejected the recitation of "such proteins" and "such protein" in items a) and b) of claim 19. Applicants traverse and submit that claim 19 has been amended to clarify that the "such proteins" and the "such protein" are to "fusion protein" in both instances. Accordingly, this rejection is moot.

Fifth, the Examiner has rejected claim 20 for the recitation of "or derivatives thereof." Applicants submit that this phrase has been removed from claim 20.

Sixth, the Examiner has rejected claim 21 for the recitation of "the detergent-based ATPS" asserting that there is insufficient antecedent basis. Applicants traverse and submit that claim 21 has been amended to recite the full name of "aqueous two-phase system" instead of ATPS. Thus, proper antecedent basis exists in claim 21 based upon claim 20.

Seventh and lastly, the Examiner points out that claim 22 sets forth a Markush group but contains only one element. Applicants submit that claim 22 has been amended accordingly.

In view of the above, Applicants respectfully submit that the present claims are fully definite. Reconsideration and withdrawal thereof of all rejections under 35 U.S.C. § 112, second paragraph are requested.

Issues Under 35 U.S.C. § 102(b)

The Examiner has rejected claim 1 under 35 U.S.C. § 102(b) as being anticipated by Kohler et al., Biotech (1991) 9, 642-646 (hereinafter referred to as Kohler). Applicants respectfully traverse this rejection.

The Examiner asserts that Kohler discloses a method of separating proteins in ATPS comprising (i) preparing a fusion polypeptide comprising part of hydrophobin-like protein (i.e. tryptophan-rich oligopeptide) and protein of interest, and (ii) subjecting said fusion protein to the ATPS-mediated protein separation. Thus, the Examiner asserts that the language "hydrophobin-like proteins and parts thereof" in particular the "parts" of the "hydrophobin-like proteins" read upon the tryptophan-rich oligopeptide of Kohler. Applicants respectfully disagree.

Applicants note that the Examiner infers that "tryptophan tags" or tryptophan-rich oligopeptides described in Kohler anticipate the claimed "parts" of the present hydrophobin-like proteins. This is not generally accepted by the understanding in the art. The specification states that hydrophobins do not usually contain tryptophan (page 7, line 28). Further, one of the inventors, Dr. Nakari-Setälä has now reviewed all the hydrophobin sequences available in public databases, and her findings confirm this understanding. She found only four (4) (from a total of 72) hydrophobins, which include one Trp residue, namely

HCF-6 in its amino terminus,

SC6 in its amino terminus,

Le.HYD1 in its amino terminus, and

HYDPt-1 prior to its last Cys residue, of which HCF-6 is a Class II hydrophobin and the others are Class I hydrophobins. None of the hydrophobins contained the tryptophan tag motif (AlaTrpTrpPro)₁₋₃ disclosed by Kohler.

In view of the above finding concerning the almost total non-existence of tryptophan in hydrophobins and the total lack of correspondence between the "tryptophan tags" of Kohler and the present claims, Applicants respectfully submit that there is no anticipation. The small prior known peptides comprising the tryptophan tag motif are quite different from the hydrophobins, hydrophobin-like proteins or parts thereof, as defined in the present invention. Therefore, Applicants submit that the present invention is not be anticipated by Kohler.

Accordingly, Applicants respectfully submit that the tryptophan tag motif disclosed by Kohler is distinct from the presently claimed hydrophobin, hydrophobin-like proteins and parts thereof. Thus, this rejection is moot. Additionally, Applicants draw the Examiner's attention to newly added claims 25-27 which further distinguish from the disclosure of Kohler.

The Examiner has also rejected claims 1 and 23 under 35 U.S.C. § 102(b) as being anticipated by Lang et al., USP 5,304,310

(hereinafter referred to as Lang). Applicants respectfully traverse this rejection.

In Lang, hirudin or a hirudin fusion protein is located in the water phase when the two phases are separated. However, Lang has a different phase system than that currently claimed. The system of Lang comprises an organic solvent as one of the phase components. Another difference is that the separation of phases is based on salts and pH, not on the characteristics of the proteins themselves. This fact is clearly shown in Example 2 of Lang. Therein, when the conditions are changed (pH is decreased) and hirudin concentrates in the organic phase instead of the aqueous phase. The Examiner states in the Office Action (last paragraph of page 8) that "hirudin mediated partitioning in organic (hydrophobic) phase can be achieved via adjusting pH value before the addition of salt." Applicants agree with the statement that "the partitioning is achieved via adjusting pH." However, Applicants disagree that the partitioning is "hirudin-mediated", since it is clearly achieved by merely changing the pH.

While it is true that the organic phase is the hydrophobic one in an aqueous/organic phase system, this fact is unrelated to the present invention. Those of skill in the art understand that organic solvents are hazardous to proteins (also discussed in Lang,

see column 1, lines 39-40 and column 3, lines 10-11 and 47-49, describing protein precipitation (denaturation) in the interphase). Lang do not exemplify separating hirudin or hirudin fusions in an ATPS (aqueous two-phase system), which is a system based on two aqueous phases, not on an aqueous and an organic phase. Lang have not tested hirudin in ATPS, and therefore it has not been shown that hirudin would separate in ATPS in a similar way as hydrophobins do.

It should also be noted that the present application does not claim a water-organic phase separation for hydrophobins. In the present method hydrophobins selectively concentrate in one of the phases (usually the lighter phase), and the phases are separated by centrifugation, not on the basis of the aqueous/organic characters of the liquids present. Accordingly, Applicants respectfully submit that the present claims are distinguished from the disclosure of Lang. Reconsideration and withdrawal of this rejection are respectfully requested.

In view of the above, Applicants respectfully submit that the present claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections is respectfully requested.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to

Appl. No. 09/936,823


November 16, 2004 in which to file a reply to the Office Action. The required fee of \$430.00 is enclosed herewith.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Reg. No. 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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